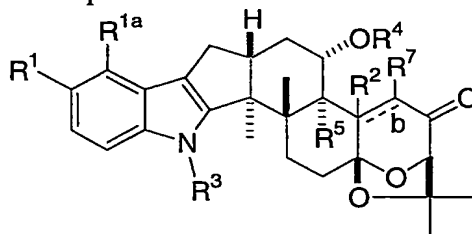


WHAT IS CLAIMED IS:

1. A compound of structural formula I:



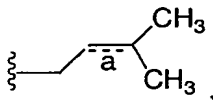
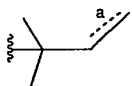
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I

or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or mixture thereof, wherein,

R¹ and R^{1a} independently are:

10

- (a) H,
 (b) C₁₋₆ alkyl
 (c) , or
 (d)  ;

15 R² is:

- (a) CO₂C₁₋₆alkyl,
 (b) H,
 (c) OH, or
 (d) C₁₋₆alkyl,

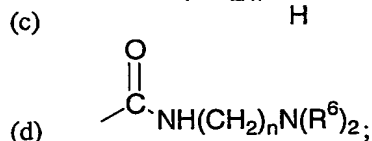
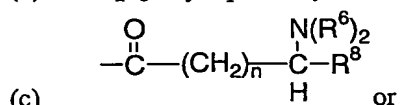
20 when a double bond is not present at b;

R³ is:

- (a) H,
 (b) (C=O)OC₁₋₆alkyl or
 25 (c) C₁₋₆alkyl optionally substituted with OH, N(R⁶)₂, or CO₂R⁶;

R⁴ is

- (a) H, provided that R³ is not H,
 (b) C₁-6alkyl optionally substituted with OH, N(R⁶)₂, or CO₂R⁶ or



5

R⁵ is:

- (a) H,
 (b) OH, or
 (c) OC₁-6alkyl;

10

R⁶ is:

- (a) H, or
 (b) C₁-6alkyl;

15

R⁷ is H, or C₁-6alkyl optionally substituted with OH, N(R⁶)₂, or CO₂R⁶;

R⁸ is H, C₁-6alkyl, CH₂-phenyl, CH₂-hydroxyphenyl, CH₂-indolyl, CH₂-imidazolyl,
 CH₂OR⁶, CH(OR⁶)CH₃, (CH₂)_nC(O)NR⁶, (CH₂)_nCO₂R⁶, (CH₂)_nSR⁶,
 (CH₂)_n(N+R⁶)₃,

20

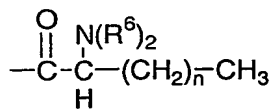
n is 0-4, and

--- is a double bond optionally and independently present at a or b.

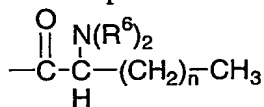
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2. A compound according to claim 1 wherein R¹, R^{1a} and R³ are hydrogen.

3. A compound according to claim 1 wherein R⁴ is

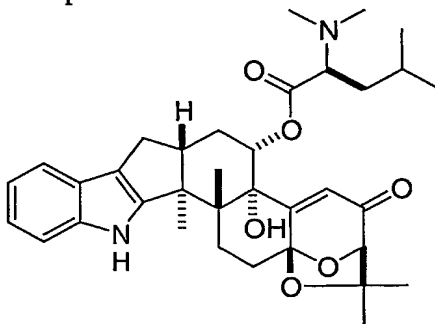


4. A compound according to claim 1 wherein R² and R⁷ are



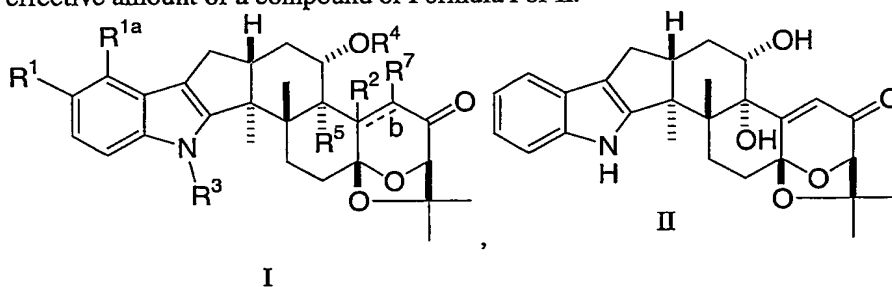
- 5 hydrogen and R⁴ is

5. A compound which is :



- 10 or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or mixture thereof.

6. A method for treating ocular hypertension or glaucoma which comprises administering to a patient in need of such treatment a therapeutically effective amount of a compound of Formula I or II:

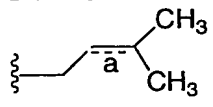
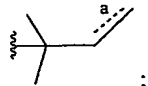


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- or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or mixture thereof:

wherein,

R¹ and R^{1a} independently are:

- 5 (a) H,
 (b) C₁₋₆ alkyl
 (c)  , or
 (d)  ;

R² is:

- 10 (a) CO₂C₁₋₆alkyl,
 (b) H,
 (c) OH, or
 (d) C₁₋₆alkyl,

when a double bond is not present at b;

15

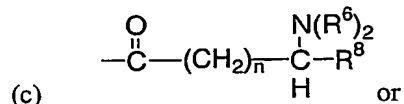
R³ is:

- (a) H,
 (b) (C=O)OC₁₋₆alkyl or
 (c) C₁₋₆alkyl optionally substituted with OH, N(R⁶)₂, or CO₂R⁶;

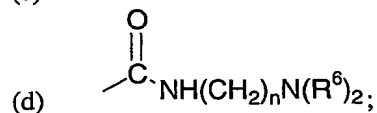
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R⁴ is

- (a) H,
 (b) C₁₋₆alkyl optionally substituted with OH, N(R⁶)₂, or CO₂R⁶ or



25



R⁵ is:

- (a) H,

- (b) OH, or
- (c) OC₁₋₆alkyl;

R⁶ is:

- 5 (a) H, or
- (b) C₁₋₆alkyl;

R⁷ is H, or C₁₋₆alkyl optionally substituted with OH, N(R⁶)₂, or CO₂R⁶;

- 10 R⁸ is H, C₁₋₆alkyl, CH₂-phenyl, CH₂-hydroxyphenyl, CH₂-indolyl, CH₂-imidazolyl, CH₂OR⁶, CH(OR⁶)CH₃, (CH₂)_nC(O)NR⁶, (CH₂)_nCO₂R⁶, (CH₂)_nSR⁶, (CH₂)_n(N⁺R⁶)₃,

n is 0-4 and

15

-- is a double bond optionally and independently present at a or b.

7. The method according to Claim 6 wherein the compound of formula I is applied as a topical formulation in the form of a solution or suspension.

20

8. The method of Claim 7, which comprises administering a second active ingredient, concurrently or consecutively, wherein the second active ingredient is a hypotensive agent selected from a β-adrenergic blocking agent, adrenergic agonist, a parasympathomimetic agent, a carbonic anhydrase inhibitor, an EP4 agonist and a prostaglandin or a prostaglandin derivative.

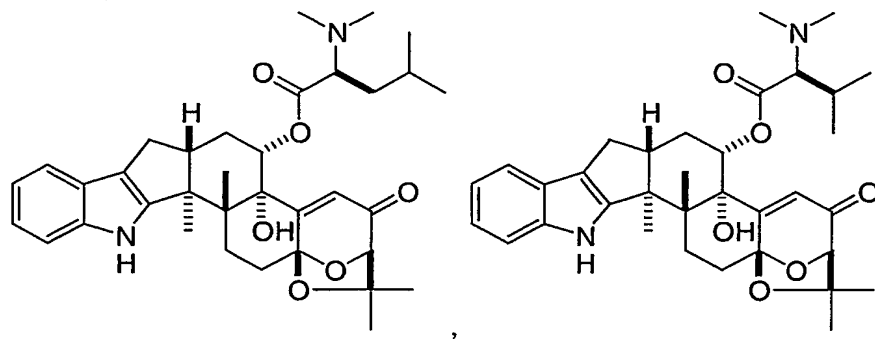
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9. The method according to claim 8 wherein the β-adrenergic blocking agent is timolol, levobunolol, carteolol, optipranolol, metapranolol or betaxolol; the parasympathomimetic agent is pilocarpine, carbachol, or phospholine iodide; adrenergic agonist is iopidine, brimonidine, epinephrine, or dipivephrin, the carbonic anhydrase inhibitor is dorzolamide, acetazolamide, metazolamide or brinzolamide; the prostaglandin is latanoprost or rescala, and the prostaglandin derivative is a hypotensive lipid derived from PGF₂α prostaglandins.

30

10. A method according to claim 7 in which the topical formulation contains xanthan gum or gellan gum.

11. A method according to claim 6 wherein the compound of formula I is:



or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or mixture thereof.

12. A method for treating macular edema, macular degeneration, or for providing a neuroprotective effect, which comprises administering to a patient in need of such treatment a pharmaceutically effective amount of a compound as recited in claim 6.

13. The method according to Claim 12 wherein the compound of formula I is applied as a topical formulation in the form of a solution or suspension.

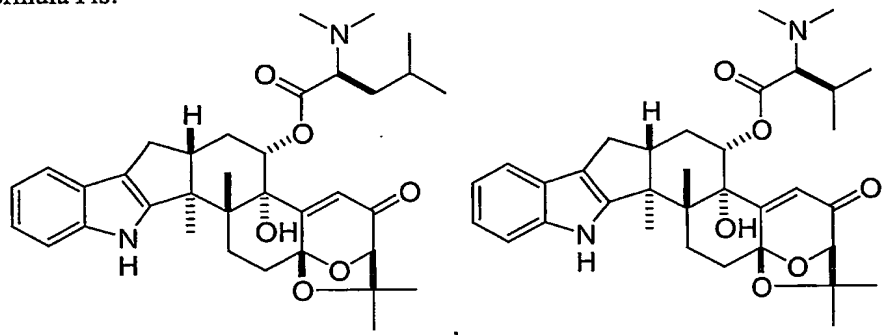
14. The method of Claim 13, which comprises administering a second active ingredient, concurrently or consecutively, wherein the second active ingredient is a hypotensive agent selected from a β -adrenergic blocking agent, adrenergic agonist, a parasympathomimetic agent, a carbonic anhydrase inhibitor, an EP4 agonist and a prostaglandin or a prostaglandin derivative.

15. The method according to claim 14 wherein the β -adrenergic blocking agent is timolol, levobunolol, carteolol, optipranolol, metapranolol or betaxolol; the parasympathomimetic agent is pilocarpine, carbachol, or phospholine

iodide; adrenergic agonist is iopidine, brimonidine, epinephrine, or dipivephrin, the carbonic anhydrase inhibitor is dorzolamide, acetazolamide, metazolamide or brinzolamide; the prostaglandin is latanoprost or rescala, and the prostaglandin derivative is a hypotensive lipid derived from PGF2 α prostaglandins.

- 5 16. A method according to claim 12 in which the topical formulation contains xanthan gum or gellan gum.

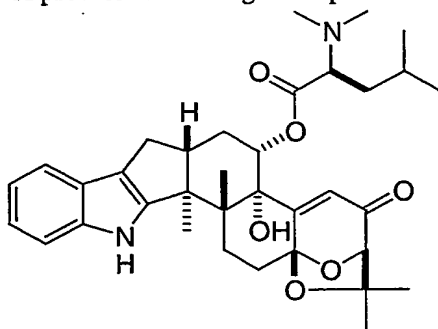
17. A method according to claim 13 wherein the compound of formula I is:



or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or mixture thereof.

- 15 18. A composition comprising a compound of formula I as recited in claim 1 and a pharmaceutically acceptable carrier.

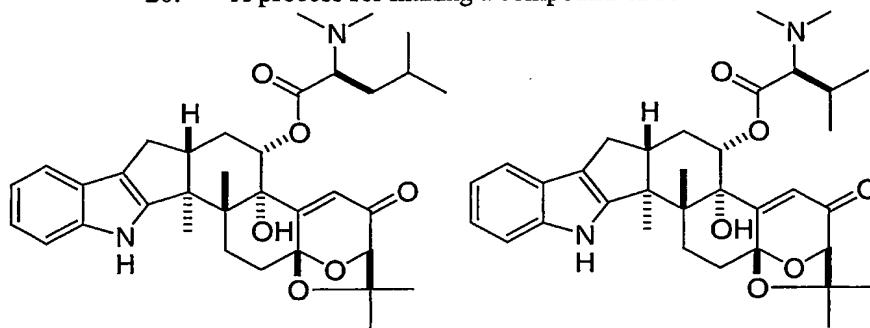
19. A process for making a compound of the formula Ia:



Ia

- or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or mixture thereof, using microbiological strain *Aspergillus alliaceus* (ATCC No. 16891 or PTA-4210), *Aspergillus nomius* (ATCC No. 15546 or PTA-4211), or *Aspergillus nomius* (ATCC No. PTA-4212).

20. A process for making a compound of the formula Ia or Ib:

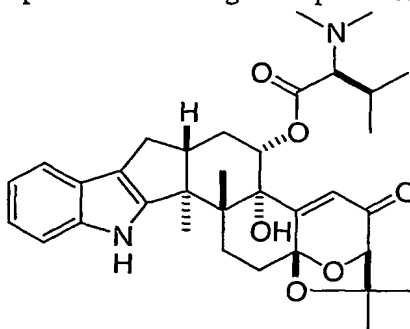


Ia

Ib

- or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or mixture thereof, using microbiological strain *Aspergillus nomius* ATCC No. 15546 (PTA-4211).

21. A process for making a compound of the formula Ib:



Ib

- or a pharmaceutically acceptable salt, enantiomer, diastereomer, tautomer or
5 mixture thereof, using microbiological strain *Aspergillus nomius* ATCC No. PTA-
4212.